

Serial No.: 09/944,161  
Filed: September 30, 2001

REMARKS

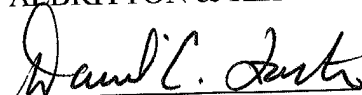
Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made."

These amendments are made in adherence with 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disc containing the above named sequence, SEQUENCE ID NUMBERS 1-13, in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "Patent-In" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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Serial No.: 09/944,161  
Filed: September 30, 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph starting on page 62, line 18, has been amended as follows:

--DNA-probe preparation: Two DNA probes for measure the wild type Cystic Fibrosis gene and the  $\Delta F508$  mutation of the Cystic Fibrosis were synthesised (DNA Technology, Aarhus, Denmark), both capture DNA-probe being 5 thiol modified.

PROBE <sub>WCF</sub> (SEQ ID NO: 1)	5' DMT-S-(CH <sub>2</sub> ) <sub>12</sub> CCATTAAAGAAAATATCATCTT-3'
PROBE <sub>ACF</sub> (SEQ ID NO: 2)	5' DMT-S-(CH <sub>1</sub> ) <sub>12</sub> GCACCATTAAAGAAAATATCATCGG-3'

Table I: Capture probe wild type = PROBE<sub>WCF</sub> and Capture probe  $\Delta F508$  mutation = PROBE<sub>ACF</sub>

The paragraph starting on page 65, line 4, has been amended as follows:

--The detection of the  $\Delta F508$  mutation of the Cystic Fibrosis gene using the PCR based micro-cantilevers as a sensor can be divided into several procedures:

1. Cleaning the gold micro-cantilever
2. Immobilization of the detection probe to the surface of the micro-cantilever (programming of the micro-cantilever chip).
3. DNA isolation from the biological sample (in this example three patient samples).

Serial No.: 09/944,161

Filed: September 30, 2001

4. Designing PCR primers for either single reactions or multiplex reactions.
5. The reaction step involving simultaneously PCR reaction probe hybridization and a 3' extension reaction.
6. Measuring the bending of the micro-cantilever due to specific extension of the probe on the surface of the micro-cantilevers.

Primer 1 <sub>CF</sub> (SEQ ID NO: 3)	5'-AAGCAAGAATATAAGACATTGG-3' (sense)
Primer 2 <sub>CF</sub> (SEQ ID NO: 4)	5'-CTATATTCATCATAGGAAACAC-3' (antisense)
PROBE <sub>WCF</sub> (SEQ ID NO: 1)	5' DMT-S-(CH <sub>2</sub> ) <sub>12</sub> -CCATTAAAGAAAATATCATCTT-3'
PROBE <sub>ACF</sub> (SEQ ID NO: 2)	5' DMT-S-(CH <sub>2</sub> ) <sub>12</sub> -GCACCATTAAAGAAAATATCATCGG-3'

Table II: Hybridization probes and PCR primers-

The paragraph starting on page 68, line 9, has been amended as follows:

---The cleaning of the gold micro- cantilever was performed as described in example 1. The quantitative analysis by RT-PCR can be difficult because of the exponential nature of PCR. A small variation during the assay might yield a marked change in the amount of the final products. The use of internal standards is therefor desirable in quantitative RT-PCR analysis to correct variations in RT-PCR as well as product detection step (micro-cantilever detection). An ideal endogenous standard would be a transcript in which the expression is constant during the cell cycle, between cell types or in response to external stimuli. A housekeeping gene GAPD that is transcribed constitutively in most cell types and tissue has been commonly used as an invariant control.

Serial No.: 09/944,161  
 Filed: September 30, 2001

PROBE <sub>IL6</sub> (SEQ ID NO:5)	5' DMT-S-(CH <sub>2</sub> ) <sub>12</sub> -CTGCGCAGCTTTAAGGAGTTCC-3'
PROBE <sub>GAPD</sub> (SEQ ID NO:6)	5' DMT-S-(CH <sub>2</sub> ) <sub>12</sub> -CGCTGGGGCTGGCATTGCCCTC-3'
Primer 1 <sub>GAPD</sub> (SEQ ID NO:7)	5'- CATCAAGAAGGTGGTGAAGC-3' (sense)
Primer 2 <sub>GAPD</sub> (SEQ ID NO:8)	5'- GAGCTTGACAAAGTGGTCGT-3' (antisense)
Primer 1 <sub>IL6</sub> (SEQ ID NO:9)	5'-ATGAACTCCTTCTCCACAAGCGC-3' (sense)
Primer 2 <sub>IL6</sub> (SEQ ID NO:10)	5'- GAAGAGCCCTCAGGCTGGACTG - 3' antisense)

Table IV: Hybridization probes and PCR primers, both probes are located in close distance to PCR Primer 2<sub>IL6</sub> and Primer 2<sub>GAPD</sub> as illustrated in figure 17 and 18.-

The paragraph starting on page 71, line 18, has been amended as follows:

--The cleaning of the gold micro-cantilever was performed as described in example 1.

PROBE <sub>HSV</sub> (SEQ ID NO:11)	5' DMT-S-(CH <sub>2</sub> ) <sub>12</sub> -CAGCAAGATAAAGGTGAACGGC-3'
Primer 1 <sub>HSV</sub> (SEQ ID NO:12)	5'-ATCAACTTCGACTGGCCCTTC-3' (sense)
Primer 2 <sub>HSV</sub> (SEQ ID NO:13)	5'-CCGTACATGTCGATGTTACAC-3' (antisense)

Table VI: Hybridization probes and PCR primers. The PCR primer give a 179 bp fragment of the HSV polymerase gene, the HSV probe are located in close distance to Primer 2<sub>HSV</sub>--

**Serial No.:** 09/944,161

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On page 73, immediately preceding the claims, the enclosed text entitled "SEQUENCE LISTING" was inserted into the text.